

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Currently amended) A method of identifying a candidate beta catenin pathway modulating agent, said method comprising the steps of:

(a) providing an assay system comprising a Polo Like Kinase 4 (PLK4) polypeptide or nucleic acid, wherein the assay system comprises cultured cells that express the PLK4 polypeptide and have defective beta-catenin function and wherein the assay system is capable of detecting the activity or expression of PLK4;

(b) contacting the assay system with a test agent; and

(c) determining the activity or expression of the PLK4 polypeptide or nucleic acid in the assay system in the presence or absence of the test agent of step (b), wherein a change in PLK4 activity or expression between the presence and absence of the test agent identifies the test agent as a candidate beta catenin pathway modulating agent.

2. – 3. (Canceled)

4. (Withdrawn) The method of Claim 1 wherein the assay system includes a screening assay comprising a PLK polypeptide, and the candidate test agent is a small molecule modulator.

5. (Withdrawn) The method of Claim 4 wherein the assay is a kinase assay.

6. (Original) The method of Claim 1 wherein the assay system is selected from the group consisting of an apoptosis assay system, a cell proliferation assay system, an angiogenesis assay system, and a hypoxic induction assay system.

7. (Withdrawn) The method of Claim 1 wherein the assay system includes a binding assay comprising a PLK polypeptide and the candidate test agent is an

antibody.

8. (Previously presented) The method of Claim 1 wherein the assay system includes an expression assay comprising a PLK4 nucleic acid and the candidate test agent is a nucleic acid modulator.

9. (Original) The method of claim 8 wherein the nucleic acid modulator is an antisense oligomer.

10. (Previously presented) The method of Claim 8 wherein the nucleic acid modulator is a phosphothioate morpholino oligomer (PMO).

11. (Withdrawn) The method of Claim 1 additionally comprising:

(d) administering the candidate beta catenin pathway modulating agent identified in (c) to a model system comprising cells defective in beta catenin function and, detecting a phenotypic change in the model system that indicates that the beta catenin function is restored.

12. (Withdrawn) The method of Claim 11 wherein the model system is a mouse model with defective beta catenin function.

13. (Withdrawn) A method for modulating a beta catenin pathway of a cell comprising contacting a cell defective in beta catenin function with a candidate modulator that specifically binds to a PLK polypeptide, whereby beta catenin function is restored.

14. (Withdrawn) The method of claim 13 wherein the candidate modulator is administered to a vertebrate animal predetermined to have a disease or disorder resulting from a defect in beta catenin function.

15. (Withdrawn) The method of Claim 13 wherein the candidate modulator is selected from the group consisting of an antibody and a small molecule.

16. (Currently amended) ~~The method of Claim 1, comprising the additional steps of~~ A method of identifying a candidate beta catenin pathway modulating agent, said method comprising the steps of:

(a) providing a first assay system comprising a Polo Like Kinase 4 (PLK4) polypeptide or nucleic acid, wherein the assay system comprises cultured cells that express the PLK4 polypeptide and wherein the assay system is capable of detecting the activity or expression of PLK4;

(b) contacting the assay system with a test agent;

(c) determining the activity or expression of the PLK4 polypeptide or nucleic acid in the assay system in the presence or absence of the test agent of step (b), wherein a change in PLK4 activity or expression between the presence and absence of the test agent identifies the test agent as a candidate beta catenin pathway modulating agent;

(d) providing a second assay system comprising cultured cells ~~or a non-human animal~~ expressing PLK4 capable of detecting a change in the beta catenin pathway,

(e) contacting the second assay system with the test agent of step (b); and

(f) measuring the beta catenin pathway in the presence or absence of the test agent, wherein the beta catenin pathway is measured by measuring the transcriptional activation of transcription factor (TCF) target genes or by measuring the transcriptional activation of beta catenin and wherein the detection of a difference in the presence and absence of the test agent confirms the test agent as a candidate beta catenin pathway modulating agent.

17. (Currently amended) The method of Claim 16 wherein the first assay system and/or the second assay system comprises cultured cells having defective beta catenin function.

18. (Withdrawn) The method of Claim 16 wherein the secondary assay system comprises a nonhuman animal.

19. (Withdrawn) The method of Claim 18 wherein the non-human animal mis-expresses a beta catenin pathway gene.

20. (Withdrawn) A method of modulating beta catenin pathway in a mammalian cell comprising contacting the cell with an agent that specifically binds a PLK polypeptide or nucleic acid.

21. (Withdrawn) The method of Claim 20 wherein the agent is administered to a mammalian animal predetermined to have a pathology associated with the beta catenin pathway.

22. (Withdrawn) The method of Claim 20 wherein the agent is a small molecule modulator, a nucleic acid modulator, or an antibody.

23. (Withdrawn) A method for diagnosing a disease in a patient comprising:
obtaining a biological sample from the patient;
contacting the sample with a probe for PLK expression;
comparing results from step (b) with a control;
determining whether step (c) indicates a likelihood of disease.

24. (Withdrawn) The method of claim 23 wherein said disease is cancer.

25. (Withdrawn) The method according to claim 24, wherein said cancer is a cancer as shown in Table 1 as having >25% expression level.